REMARKS

Applicants thank the Office for the attention accorded the present Application in the March 23, 2007, Office Action. In that Action, Claims 8-11 were rejected under 35 USC §102(b) as being anticipated by Pepine (American Journal of Cardiology No. 77) and Claims 1-7 and 14 were rejected under 35 USC §103(a) as being unpatentable over Powell et al.(US 6,140,319) and Pepine. Applicants respectfully traverse.

Applicants are submitting herewith a Supplemental Information Disclosure Statement with the appropriate fee for consideration.

In light of the Supplemental Information Disclosure Statement, Applicants have canceled Claims 1-14 and added new Claims 15-20 that are drawn to a method of secondary cardiovascular prevention in a hypertensive and a non-hypertensive patient. A total of 6 claims containing 4 independent claims are now pending in the application. Where Applicants have already paid the fee for the additional independent claim, no additional fees are requires.

Support for the new claims can be found in Applicants' disclosure in Paragraphs [0003], [0004], [0006], [0007], [0008], [0012], and [0015].

35 USC §102(b) rejections:

The Office has rejected Claims 8-11 under 35 USC §102(b) as being anticipated by Pepine. The Office states that Pepine teaches that aspirin and beta-blockers are an important part of attempting to influence prognosis of CAD patients, especially after myocardial infarction. Applicants respectfully traverse.

Pepine fails to teach the combination of any of the medications disclosed as a single dosage unit. In fact, Pepine discloses that an important part of attempting to influence prognosis in CAD patients is assurance that the drugs are actually being used. (See Pge 5D). Pepine states that this requires physician prescription in appropriate doses and patient adherence with the prescription. Pepine admits that these processes are very complicated and related to both physician and patient education, awareness of disease, and beneficial effects of drugs as well as physician prescribing patterns and patient compliance. Pepine concludes that even though aspirin and beta-blockers have been proven to improve prognosis in CAD patients, studies of patient use show disappointing results. (See Page 5D, 2nd Column). Further, Pepine fails to disclose a method of secondary cardiovascular prevention in hypertensive and non-hypertensive individuals using a single dosage unit.

In light of the above amendments and arguments, Applicants respectfully submit that the 35 USC §102(b) rejection of Claims 8-11 has been successfully traversed and that Applicants' new claims are also patentably distinct over Pepine for the same reasons. Allowance is therefore requested.

35 USC §103(a) rejection:

The Office has rejected Claims 1-7 and 12-14 under 35 USC §103(a) as being unpatentable over Powell et al. and Pepine.

The Office states that Powell et al. teach a single dosage unit of a vasopeptidase inhibitor combined with a beta-blocker and an antiplatelet agent where the difference is

the inclusion of a vasopeptidase inhibitor. The Office further states that absent a clear indication in the specification or claims of the basic and novel characteristics of the present invention, the transition phrase "consisting essentially of" will be construed as equivalent to "comprising" and that the Applicants have the burden of showing that the introduction of additional steps or components would materially change the characteristics of Applicants' invention. The Office concludes that the addition of a vasopeptidase inhibitor would not materially change the characteristics of Applicants' invention.

The Office cites Pepine for teaching the importance of treating CAD patients with aspirin and beta-blockers.

Applicants respectfully traverse.

Contrary to the Office's assertion, the addition of a vasopeptidase inhibitor would substantially change the characteristics of the present invention. Vasopeptidase inhibitor and omapatrilat, as taught by Powell et al., in combination with a beta-adrenergic blocking agent would result in a dosage unit that inherently has added risk for some individuals with cardiovascular disease.

Powell et al. discloses that vasopeptidase inhibitors possess "...in a single molecule both angiotensin converting enzyme (ACE) inhibitory activity and neural endopeptidase (EC24:11; NEP) inhibition activity" and "are also referred to as ...ACE/NEP inhibitors." (Column 1, lines 9-16).

Applicants have previously stated that the addition of a vasopeptidase inhibitor to the present invention would change the characteristics of the invention in "material,"

and in some instances "unexpected," ways. These included increased cardiac mortality and increased readmission rates. Some of these changes would not be due to effects of the vasopeptidase inhibitor itself, but rather due to interaction with aspirin and/or the beta-blocker components of the present invention. Powell et al. does not anticipate these interactions.

In addition to the previous arguments and evidence presented by Applicants, Applicants present Exhibit 1-062107 (D. Hall et al., "Counteraction of the vasodilator effects of enalapril by aspirin in severe heart failure," J. Am. Coll. Cardiol., 1992, Vol. 20, pp 1549-1555), which discloses the counteraction of the vasodilator effects of enalapril (an ACE inhibitor) by aspirin in severe heart failure. The study by D Hall et al. indicates that the prostaglandin synthesis inhibition by aspirin counteracts the systemic arterial vasodilation of angiotensin-converting enzyme inhibition with enalapril and substantiates its dependence on the integrity of prostaglandin metabolism. This study demonstrates a "material" and undesirable effect from combining aspirin, a medication of the present invention, with an ACE inhibitor. In other words, aspirin counteracts the benefits of the ACE inhibitor.

Applicants also referenced another study previously presented in Exhibit 03-83006 by K. N. Nguyen et al. and dated 1997, which reexamined a previous study by K. Swedberg et al. dated 1992 that found that aspirin was a significant predictor of increased mortality.

All three were published prior to Applicants' invention and establish what was known by those of ordinary skill in the art at the time of Applicants' invention. Yet, the

Office seems to pass over such evidence and only concentrates on the previously submitted Exhibits that were published after Applicants' filing date. The Office seems to confuse the purpose of the Exhibits provided by Applicants. To clarify, the Exhibits published before Applicants' filing date establish the material effect of combining an ACE inhibitor with aspirin. The Exhibits published after Applicants' filing date reinforce and further confirm and support the earlier findings of the material effect of the ACE inhibitor.

Applicants have pointed out substantive and material changes that would result from a vasopeptidase inhibitor-containing combination taught by Powell et al. as opposed to the present invention that (by virtue of "consisting essentially of" claim transition) would not contain a vasopeptidase inhibitor.

Such a combination would be the antithesis of protective. In view of this contradiction, Powell et al. teach the addition of an ingredient that materially affects the basic and novel characteristics of Applicants' invention.

Unlike the addition of incipients such as binders and stabilizers that have no effect on the characteristics of Applicants' invention, it is clear from the evidence submitted by Applicants that the increased risks associated with vasopeptidase inhibitors render the addition of vasopeptidase inhibitors in Applicants' invention as materially affecting the basic characteristics of Applicants' claimed invention.

The Office then relies on Pepine to teach the importance of treating CAD patients with aspirin and beta-blockers. Pepine provides no teaching that is not already disclosed in Applicants' specification under the Description of the Prior Art. Pepine

does not teach the use of a single dosage unit consisting essentially of a beta-adrenergic blocking agent and a platelet inhibitor for the secondary prevention of a heart attack in a non-hypertensive person.

With regard to the newly submitted prior art (US 5,156,849 issued to Byrne et al.), Byrne teaches a pharmaceutical composition comprising aspirin, atenolol and a barrier film coating around the atenolol. Byrne et al. also fails to disclose a method for secondary cardiovascular prevention in a non-hypertensive patient. Byrne discloses use of atenolol or any beta-blocker only for anti-hypertensive use.

In light of the amendments and arguments presented, Applicants respectfully submit that the 35 USC §103(a) rejection of Claims 1-7 and 12-14 has been successfully traversed. Allowance is therefore requested.

Applicants believe that all of the pending claims should now be in condition for allowance. Early and favorable action is respectfully requested.

The Examiner is invited to telephone the undersigned, Applicant's attorney of record, to facilitate advancement of the present application.

Respectfully submitted,

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